(FILE 'HOME' ENTERED AT 18:07:47 ON 09 JAN 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 18:07:56 ON 09 JAN 2003

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L1         12645 S C. ELEGANS
L2         28518 S C. ELEGANS OR CAENORHABDITIS
L3          4937 S L2 AND (TRAIT OR PHENOTYP? OR SCREEN?)
L4           557 S L3 AND LIBRAR?
L5           288 DUP REM L4 (269 DUPLICATES REMOVED)
L6           288 FOCUS L5 1-
L7         34508 S ELEGANS OR NEMATODE (L) PHENOTYPIC PROFILES
L8             1 S (ELEGANS OR NEMATODE) (L) PHENOTYPIC PROFILES
L9          5548 S (ELEGANS OR NEMATODE) (L) MUTANT?
L10          587 S L9 AND SCREEN?
L11          269 S L10 AND PHENOTYP?
L12          119 DUP REM L11 (150 DUPLICATES REMOVED)
L13          119 FOCUS L12 1-
L14          192 S L3 AND DAF?
L15           82 DUP REM L14 (110 DUPLICATES REMOVED)
L16           82 FOCUS L15 1-
                 E BOGAERT THIERRY?/AU
                 E BOGAERT T?/AU
L17           29 S E4
L18           28 DUP REM L17 (1 DUPLICATE REMOVED)
L19           28 SORT L18 PY
L20           23 S L19 AND L2

=> d an ti so au ab pi l20 13 15 16 18

L20  ANSWER 13 OF 23  CAPLUS  COPYRIGHT 2003 ACS
AN   2000:756909  CAPLUS
DN   133:317531
TI   Nematodes for screening of compounds with potential pharmacological
     activity
SO   PCT Int. Appl., 137 pp.
     CODEN: PIXXD2
IN   Verwaerde, Philippe; Platteeuw, Christ; Cuvillier, Gwladys; Bogaert,
     Thierry
AB   Screening methods are provided which use nematode worms, particularly but
     not exclusively Caenorhabditis elegans , which are adapted to be
     performed in a high-throughput format.
     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
PI   WO 2000063427     A2    20001026       WO 2000-IB575     20000414
     WO 2000063427     A3    20011206
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
             IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
             SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     GB 2351151        A1    20001220       GB 2000-9358      20000414
     GB 2359358        A1    20010822       GB 2001-11712     20000414
     GB 2359358        B2    20020327
     GB 2359359        A1    20010822       GB 2001-11713     20000414
     GB 2359359        B2    20020123
     GB 2359360        A1    20010822       GB 2001-11783     20000414
     GB 2359360        B2    20020116
     GB 2359361        A1    20010822       GB 2001-11787     20000414
     GB 2359361        B2    20020116
     GB 2359626        A1    20010829       GB 2001-11714     20000414
     GB 2359626        B2    20020501
     GB 2359627        A1    20010829       GB 2001-11778     20000414
     GB 2359627        B2    20020123
     EP 1175506        A2    20020130       EP 2000-920972    20000414
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
```

JP 2002542466 T2 20021210 JP 2000-612504 20000414

L20 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2000:756907 CAPLUS
DN 133:317530
TI Drug screening using modified nematode worms
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN Verwaerde, Philippe; Feichtinger, Richard; Beghyn, Myriam; **Bogaert, Thierry**
AB The invention provides methods of screening compds. for potential pharmacol. activity using nematode worms, principally but not exclusively, the nematode **Caenorhabditis** elegans. Specifically, the invention relates to the use of nematodes modified to have certain characteristics which provide advantages for compd. screening, such as constitutive pharyngeal pumping, increased gut permeability or altered gut mol. transport. Methods for selecting suitably modified nematodes from a population of nematodes are also provided.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000063425	A2	20001026	WO 2000-IB557	20000414
WO 2000063425	A3	20010308		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2351152	A1	20001220	GB 2000-9360	20000414
GB 2351152	B2	20010725		
GB 2358399	A1	20010725	GB 2001-9262	20000414
GB 2358399	B2	20020116		
GB 2358400	A1	20010725	GB 2001-9263	20000414
GB 2358400	B2	20020116		
EP 1169472	A2	20020109	EP 2000-919101	20000414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002542465	T2	20021210	JP 2000-612502	20000414

L20 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2000:756906 CAPLUS
DN 133:317529
TI Method for screening compounds using nematode worms
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
IN Feichtinger, Richard; Rottiers, Veerle; **Bogaert, Thierry**; Maillet, Isabelle
AB The invention provides improved methods of screening compds. for potential pharmacol. activity using nematode worms, principally but not exclusively, **Caenorhabditis** elegans. Specifically, the invention relates to methods in which the test compd. is added directly to a nematode food source organism (e.g. a microorganism) and therefore taken up by the nematodes during feeding.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000063424	A2	20001026	WO 2000-IB554	20000414
WO 2000063424	A3	20010208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2350896	A1	20001213	GB 2000-9364	20000414

GB 2350896 B2 20010425
EP 1169471 A2 20020109 EP 2000-919099 20000414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002542464 T2 20021210 JP 2000-612501 20000414

L20 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2000:401965 CAPLUS
DN 133:28275
TI Method for constructing libraries of phenotypic profiles in nematode worm
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
IN Kaletta, Titus; Feichtinger, Richard; Van Poucke, Jonas; Van Geel, Anton; Appelmans, Saskia; Van Criekinge, Wim; **Bogaert, Thierry**
AB Methods are provided for use in constructing libraries of phenotypic profiles in a nematode worm such as **Caenorhabditis** elegans. The methods require measurement of identifiable characteristics of the worm and systematic scoring of these characteristics. Also provided are methods of identifying compds. with potential pharmacol. activity, for detg. the mode of action of a given compd. and for assigning genes to particular biochem. pathways.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000034438	A2	20000615	WO 1999-EP9710	19991207
WO 2000034438	A3	20001109		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1137754 A2 20011004 EP 1999-963460 19991207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002531115 T2 20020924 JP 2000-586872 19991207

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L2 28518 S C. ELEGANS OR CAENORHABDITIS
L3 4937 S L2 AND (TRAIT OR PHENOTYP? OR SCREEN?)
L4 557 S L3 AND LIBRAR?
L5 288 DUP REM L4 (269 DUPLICATES REMOVED)
L6 288 FOCUS L5 1-
L7 34508 S ELEGANS OR NEMATODE (L) PHENOTYPIC PROFILES
L8 1 S (ELEGANS OR NEMATODE) (L) PHENOTYPIC PROFILES

=> d an ti so au ab pi l8

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2000:401965 CAPLUS
DN 133:28275
TI Method for constructing libraries of **phenotypic profiles** in **nematode** worm
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
IN Kaletta, Titus; Feichtinger, Richard; Van Poucke, Jonas; Van Geel, Anton; Appelmans, Saskia; Van Criekinge, Wim; Bogaert, Thierry
AB Methods are provided for use in constructing libraries of **phenotypic profiles** in a **nematode** worm such as Caenorhabditis **elegans**. The methods require measurement of identifiable characteristics of the worm and systematic scoring of these characteristics. Also provided are methods of identifying compds. with potential pharmacol. activity, for detg. the mode of action of a given compd. and for assigning genes to particular biochem. pathways.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000034438	A2	20000615	WO 1999-EP9710	19991207
WO 2000034438	A3	20001109		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1137754	A2	20011004	EP 1999-963460	19991207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531115	T2	20020924	JP 2000-586872	19991207

6 ANSWER 1 OF 288 CAPLUS COPYRIGHT 2003 ACS
AN 2000:401965 CAPLUS
DN 133:28275
TI Method for constructing **libraries** of **phenotypic** profiles in nematode worm
IN Kaletta, Titus; Feichtinger, Richard; Van Poucke, Jonas; Van Geel, Anton; Appelmans, Saskia; Van Criekinge, Wim; Bogaert, Thierry
PA Devgen N.V., Belg.
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N001-04
ICS C12N001-00; C12N015-01; C12N015-10
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 3, 12, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000034438	A2	20000615	WO 1999-EP9710	19991207
	WO 2000034438	A3	20001109		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1137754	A2	20011004	EP 1999-963460	19991207
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002531115	T2	20020924	JP 2000-586872	19991207
PRAI	GB 1998-26890	A	19981207		
	WO 1999-EP9710	W	19991207		

AB Methods are provided for use in constructing **libraries** of **phenotypic** profiles in a nematode worm such as **Caenorhabditis** elegans. The methods require measurement of identifiable characteristics of the worm and systematic scoring of these characteristics. Also provided are methods of identifying compds. with potential pharmacol. activity, for detg. the mode of action of a given compd. and for assigning genes to particular biochem. pathways.
ST constructing **library phenotype** nematode worm gene; pharmacol **phenotype library Caenorhabditis**
IT Neurotransmission
(GABAergic; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Electric potential
pH
(change in; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Chemistry
(chem. compds., effect of; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Neurotransmission
(cholinergic; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Stress, animal
(cold; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Combinatorial **library**
(effect of compds. of; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Virus
(exposure to; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Bacteria (Eubacteria)
Escherichia coli
(feeding worm on; method for constructing **libraries** of

phenotypic profiles in nematode worm)
IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(green fluorescent, as reporter; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Stress, animal
(heat; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Microscopy
(interference; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Gene, microbial
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lacZ, as reporter gene; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Stress, animal
(light; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT **Caenorhabditis** elegans
Calorimetry
Drug **screening**
Fluorescence microscopy
Fluorometry
Genome
Genomic **library**
Immunoassay
Libraries
Luminescence spectroscopy
Metabolic pathways
Microscopy
Mutation
Pharmacology
Phenotypes
Radiochemical analysis
Spectrophotometry
Stress, animal
Worm
(method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Transgene
RL: ADV (Adverse effect, including toxicity); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Gene, animal
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Reporter gene
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Stress, animal
(osmotic; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Drugs
(target; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT Disease, animal
(transgene assocd. with, of human; method for constructing **libraries** of **phenotypic** profiles in nematode worm)
IT 9000-81-1, Acetylcholine esterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, **phenotypes** induced by; method for constructing

libraries of **phenotypic** profiles in nematode worm)

L13 ANSWER 3 OF 119 CAPLUS COPYRIGHT 2003 ACS
AN 2002:315204 CAPLUS
DN 136:336183
TI Methods for identifying pesticidal compds. using gene sca-1 for sarco-endoplasmic reticulum Ca2+ ATPase cloned from C. elegans
SO PCT Int. Appl., 205 pp.
CODEN: PIXXD2
IN Zwaal, Richard; Kaletta, Titus; Van den Craen, Marc; Logghe, Marc; Smits, Elke; Van Creikinge, Wim; Bogaert, Thierry
AB The invention is concerned with methods for use in the identification of compds. having potential utility as pesticides. In particular, the invention relates to methods for use in identifying compds. which affect the activity of a physiol. important calcium pump, the sarco/endoplasmic reticulum Ca2+ ATPase (SERCA). In particular, gene sca-1 coding for sarco-endoplasmic reticulum Ca2+-transport ATPase (SERCA) in Caenorhabditis (C.) **elegans** (showing exon IV and V and surrounding introns plus promoter sequences) is cloned using primers designed according the conserved sequences of plant SERCA cDNA sequences. A lethal **mutant** C. **elegans** called ok190 is generated and rescue of sca-1 mutation by expression of a pest SERCA protein results in wild-type **phenotypes** of pharynx pumping, movement, egg laying, defecation, mating and etc. And inhibition of C. **elegans** SERCA activity using thapsigargin or other chem. inhibitors of SERCA results in worms with recognisable **phenotypic** characteristics, including reduced growth, reduced rate of pharynx pumping and reduced nos. of progeny. Based on these results pesticide **screening** methods are developed and disclosed using C. **elegans** or cultured mammalian cell systems.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002033405	A1	20020425	WO 2001-IB2391	20011015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002018457	A5	20020429	AU 2002-18457	20011015

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L1         12645 S C. ELEGANS
L2         28518 S C. ELEGANS OR CAENORHABDITIS
L3          4937 S L2 AND (TRAIT OR PHENOTYP? OR SCREEN?)
L4           557 S L3 AND LIBRAR?
L5           288 DUP REM L4 (269 DUPLICATES REMOVED)
L6           288 FOCUS L5 1-
L7         34508 S ELEGANS OR NEMATODE (L) PHENOTYPIC PROFILES
L8             1 S (ELEGANS OR NEMATODE) (L) PHENOTYPIC PROFILES
L9          5548 S (ELEGANS OR NEMATODE) (L) MUTANT?
L10          587 S L9 AND SCREEN?
L11          269 S L10 AND PHENOTYP?
L12          119 DUP REM L11 (150 DUPLICATES REMOVED)
L13          119 FOCUS L12 1-

=> d an ti so au ab l13 5

L13  ANSWER 5 OF 119     MEDLINE
AN   1998315096     MEDLINE
TI   A genetic screen for temperature-sensitive cell-division
     mutants of Caenorhabditis elegans.
SO   GENETICS, (1998 Jul) 149 (3) 1303-21.
     Journal code: 0374636. ISSN: 0016-6731.
AU   O'Connell K F; Leys C M; White J G
AB   A novel screen to isolate conditional cell-division
     mutants in Caenorhabditis elegans has been developed.
     The screen is based on the phenotypes associated with
     existing cell-division mutations: some disrupt postembryonic divisions and
     affect formation of the gonad and ventral nerve cord-resulting in sterile,
     uncoordinated animals-while others affect embryonic divisions and result
     in lethality. We obtained 19 conditional mutants that displayed
     these phenotypes when shifted to the restrictive temperature at
     the appropriate developmental stage. Eighteen of these mutations have been
     mapped; 17 proved to be single alleles of newly identified genes, while 1
     proved to be an allele of a previously identified gene. Genetic tests on
     the embryonic lethal phenotypes indicated that for 13 genes,
     embryogenesis required maternal expression, while for 6, zygotic
     expression could suffice. In all cases, maternal expression of wild-type
     activity was found to be largely sufficient for embryogenesis. Cytological
     analysis revealed that 10 mutants possessed embryonic
     cell-division defects, including failure to properly segregate DNA,
     failure to assemble a mitotic spindle, late cytokinesis defects, prolonged
     cell cycles, and improperly oriented mitotic spindles. We conclude that
     this approach can be used to identify mutations that affect various
     aspects of the cell-division cycle.
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L2        28518 S C. ELEGANS OR CAENORHABDITIS
L3         4937 S L2 AND (TRAIT OR PHENOTYP? OR SCREEN?)
L4          557 S L3 AND LIBRAR?
L5          288 DUP REM L4 (269 DUPLICATES REMOVED)
L6          288 FOCUS L5 1-
L7        34508 S ELEGANS OR NEMATODE (L) PHENOTYPIC PROFILES
L8            1 S (ELEGANS OR NEMATODE) (L) PHENOTYPIC PROFILES
L9         5548 S (ELEGANS OR NEMATODE) (L) MUTANT?
L10         587 S L9 AND SCREEN?
L11         269 S L10 AND PHENOTYP?
L12         119 DUP REM L11 (150 DUPLICATES REMOVED)
L13         119 FOCUS L12 1-
L14         192 S L3 AND DAF?
L15          82 DUP REM L14 (110 DUPLICATES REMOVED)
L16          82 FOCUS L15 1-
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=> d an ti so au ab pi l16 1 2 5 6 8 9

L16 ANSWER 1 OF 82 CAPLUS COPYRIGHT 2003 ACS
AN 1998:761816 CAPLUS
DN 130:29188
TI Therapeutic and diagnostic tools for impaired glucose tolerance conditions based on the dauer polypeptides and genes of **Caenorhabditis** elegans
SO PCT Int. Appl., 202 pp.
CODEN: PIXXD2
IN Ruvkun, Gary; Kimura, Koutarou; Patterson, Garth; Ogg, Scott; Paradis, Suzanne; Tissenbaum, Heidi; Morris, Jason; Koweek, Allison; Pierce, Sarah
AB Disclosed herein are novel genes and methods for the **screening** of therapeutics useful for treating impaired glucose tolerance conditions, as well as diagnostics and therapeutic compns. for identifying or treating such conditions. The **Caenorhabditis** elegans metabolic regulatory genes **daf**-2 and age-1 encode homologs of the mammalian insulin receptor/phosphoinositide 3-kinase signaling pathway proteins, resp. In addn., the **DAF**-16 forkhead protein represents the major transcriptional output of this insulin signaling pathway. Dysregulation of the **DAF**-16 transcription factor in the absence of insulin signaling leads to metabolic defects; inactivation of **DAF**-16 reverses the metabolic defects caused by lack of insulin signaling in **C. elegans**. Finally, the **C. elegans daf**-7, da-1, **daf**-4, **daf**-8, **daf**-14, and **daf**-3 genes encode neuroendocrine/target tissue transforming growth factor-.beta. type signal transduction mols. that genetically interact with the insulin signaling pathway. Metabolic defects cause by lack of neuroendocrine TGF-.beta. signals can be reversed by inactivation of the **DAF**-3 transcription factor. The **C. elegans daf** genes are excellent candidate genes and proteins for human disease assocd. with glucose intolerance, e.g., diabetes, obesity, and atherosclerosis. The human homologs of these **daf** genes and proteins mediate insulin signaling in normal people and may be defective or mis-regulated in diabetics. Moreover, there are at least 2 classes of type II diabetics: those with defects in the TGF-.beta. signaling genes, and those with defects in insulin signaling genes. Exemplary sequences and functional characteristics are provided for the **C. elegans daf** homologs of the human genes: **daf**-2, **daf**-3 (3 differentially spliced isoforms), **daf**-16 (2 differentially spliced isoforms), age-1, and pdk-1 (two spliced isoforms).

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851351	A1	19981119	WO 1998-US10080	19980515

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,

KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6225120	B1	20010501	US 1997-857076	19970515
AU 9874941	A1	19981208	AU 1998-74941	19980515
AU 752962	B2	20021003		
EP 1019092	A1	20000719	EP 1998-922382	19980515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511747	T2	20020416	JP 1998-549639	19980515
US 2001029617	A1	20011011	US 1998-205658	19981203
US 2002037585	A1	20020328	US 2001-844353	20010427

L16 ANSWER 2 OF 82 CAPLUS COPYRIGHT 2003 ACS
AN 2000:384548 CAPLUS
DN 133:39116
TI Genes and polypeptides involved in insulin signaling pathways for glucose tolerance, obesity, and longevity and their uses as therapeutic and diagnostic tools
SO PCT Int. Appl., 402 pp.
CODEN: PIXXD2
IN Ruvkun, Gary; Ogg, Scott
AB Disclosed herein are novel genes and methods for the **screening** of therapeutics useful for treating impaired glucose tolerance conditions, as well as diagnostics and therapeutic compns. for identifying or treating such conditions. The **Caenorhabditis** elegans metabolic regulatory genes **daf**-2 and age-1 encode homologs of the mammalian insulin receptor/phosphoinositol 3-kinase signaling pathway proteins, resp. Also, the **C. elegans** PKB kinase and AKT kinase act downstream of these genes, as their mammalian homologs act downstream of insulin signaling. The **C. elegans** PTEN lipid phosphatase homolog, **DAF**-18, acts upstream of AKT in this signaling pathway. Further, the **DAF**-16 forkhead protein represents the major transcriptional output of this insulin signaling pathway. Addnl. evidence indicates that the **DAF**-16, **DAF**-3, **DAF**-8, and **DAF**-14 transcriptional outputs of converging signaling pathways regulate metab. The congruence between the **C. elegans** and mammalian insulin signaling pathways strongly supports the contention that new genes identified in the **C. elegans** pathway also act in mammalian insulin signaling. Exemplary sequences and functional characteristics of the **C. elegans daf** genes and their human homologs are provided.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000033068	A1	20000608	WO 1999-US28529	19991202
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001029617	A1	20011011	US 1998-205658	19981203
EP 1163515	A1	20011219	EP 1999-960641	19991202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L16 ANSWER 5 OF 82 MEDLINE
AN 94333774 MEDLINE
TI **daf**-2, **daf**-16 and **daf**-23: genetically interacting genes controlling Dauer formation in **Caenorhabditis** elegans.
SO GENETICS, (1994 May) 137 (1) 107-20.
Journal code: 0374636. ISSN: 0016-6731.

AU Gottlieb S; Ruvkun G
AB Under conditions of high population density and low food, **Caenorhabditis** elegans forms an alternative third larval stage, called the dauer stage, which is resistant to desiccation and harsh environments. Genetic analysis of some dauer constitutive (**Daf**-c) and dauer defective (**Daf**-d) mutants has revealed a complex pathway that is likely to function in particular neurons and/or responding tissues. Here we analyze the genetic interactions between three genes which comprise a branch of the dauer formation pathway that acts in parallel to or downstream of the other branches of the pathway, the **Daf**-c genes **daf**-2 and **daf**-23 and the **Daf**-d gene **daf**-16. Unlike mutations in other **Daf**-c genes, mutations in both **daf**-2 and **daf**-23 cause non-conditional arrest at the dauer stage. Our epistasis analysis suggests that **daf**-2 and **daf**-23 are functioning at a similar point in the dauer pathway. First, mutations in **daf**-2 and **daf**-23 are epistatic to mutations in the same set of **Daf**-d genes. Second, **daf**-2 and **daf**-23 mutants are suppressed by mutations in **daf**-16. Mutations in **daf**-16 do not suppress any of the other **Daf**-c mutants as efficiently as they suppress **daf**-2 and **daf**-23 mutants. Third, double mutants between either **daf**-2 or **daf**-23 and several other **daf**-d mutants exhibit an unusual interaction. Based on these results, we present a model for the function of **daf**-2, **daf**-23 and **daf**-16 in dauer formation.

L16 ANSWER 6 OF 82 MEDLINE
AN 93387665 MEDLINE
TI Evidence for parallel processing of sensory information controlling dauer formation in **Caenorhabditis** elegans.
SO GENETICS, (1993 Aug) 134 (4) 1105-17.
Journal code: 0374636. ISSN: 0016-6731.
AU Thomas J H; Birnby D A; Vowels J J
AB Dauer formation in **Caenorhabditis** elegans is induced by chemosensation of high levels of a constitutively secreted pheromone. Seven genes defined by mutations that confer a dauer-formation constitutive **phenotype** (**Daf**-c) can be congruently divided into two groups by any of three criteria. Group 1 genes (**daf**-11 and **daf**-21) are (1) strongly synergistic with group 2 genes for their **Daf**-c **phenotype**, (2) incompletely suppressed by dauer-formation defective (**Daf**-d) mutations in the genes **daf**-3 and **daf**-5 and (3) strongly suppressed by **Daf**-d mutations in nine genes that affect the structure of chemosensory endings. Group 2 genes (**daf**-1, **daf**-4, **daf**-7, **daf**-8 and **daf**-14) are (1) strongly synergistic with group 1 genes for their **Daf**-c **phenotype**, (2) fully suppressed by **Daf**-d mutations in **daf**-3 and **daf**-5 and (3) not suppressed by **Daf**-d mutations in the nine genes that affect chemosensory ending structure. Mutations in each group of genes also cause distinct additional behavioral defects. We propose that these two groups of **Daf**-c genes act in parallel pathways that process sensory information. The two pathways are partially redundant with each other and normally act in concert to control dauer formation.

L16 ANSWER 8 OF 82 MEDLINE
AN 1998393575 MEDLINE
TI Two pleiotropic classes of **daf**-2 mutation affect larval arrest, adult behavior, reproduction and longevity in **Caenorhabditis** elegans.
SO GENETICS, (1998 Sep) 150 (1) 129-55.
Journal code: 0374636. ISSN: 0016-6731.
AU Gems D; Sutton A J; Sundermeyer M L; Albert P S; King K V; Edgley M L; Larsen P L; Riddle D L
AB The nematode **Caenorhabditis** elegans responds to overcrowding and scarcity of food by arresting development as a dauer larva, a nonfeeding, long-lived, stress-resistant, alternative third-larval stage. Previous work has shown that mutations in the genes **daf**-2 (encoding a member of the insulin receptor family) and age-1 (encoding a PI 3-kinase) result in constitutive formation of dauer larvae (**Daf**-c),

increased adult longevity (Age), and increased intrinsic thermotolerance (Itt). Some **daf**-2 mutants have additional developmental, behavioral, and reproductive defects. We have characterized in detail 15 temperature-sensitive and 1 nonconditional **daf**-2 allele to investigate the extent of **daf**-2 mutant defects and to examine whether specific mutant **traits** correlate with each other. The greatest longevity seen in **daf**-2 mutant adults was approximately three times that of wild type. The temperature-sensitive **daf**-2 mutants fell into two overlapping classes, including eight class 1 mutants, which are **Daf**-c, Age, and Itt, and exhibit low levels of L1 arrest at 25.5 degrees. Seven class 2 mutants also exhibit the class 1 defects as well as some or all of the following: reduced adult motility, abnormal adult body and gonad morphology, high levels of embryonic and L1 arrest, production of progeny late in life, and reduced brood size. The strengths of the **Daf**-c, Age, and Itt **phenotypes** largely correlated with each other but not with the strength of class 2-specific defects. This suggests that the **DAF**-2 receptor is bifunctional. Examination of the null **phenotype** revealed a maternally rescued egg, L1 lethal component, and a nonconditional **Daf**-c component. With respect to the **Daf**-c **phenotype**, the dauer-defective (**Daf**-d) mutation **daf**-12(m20) was epistatic to **daf**-2 class 1 alleles but not the severe class 2 alleles tested. All **daf**-2 mutant defects were suppressed by the **daf**-d mutation **daf**-16(m26). Our findings suggest a new model for **daf**-2, age-1, **daf**-12, and **daf**-16 interactions.

L16 ANSWER 9 OF 82 MEDLINE
AN 95309673 MEDLINE
TI Genes that regulate both development and longevity in **Caenorhabditis** elegans.
SO GENETICS, (1995 Apr) 139 (4) 1567-83.
Journal code: 0374636. ISSN: 0016-6731.
AU Larsen P L; Albert P S; Riddle D L
AB The nematode **Caenorhabditis** elegans responds to conditions of overcrowding and limited food by arresting development as a dauer larva. Genetic analysis of mutations that alter dauer larva formation (**daf** mutations) is presented along with an updated genetic pathway for dauer vs. nondauer development. Mutations in the **daf**-2 and **daf**-23 genes double adult life span, whereas mutations in four other dauer-constitutive genes positioned in a separate branch of this pathway (**daf**-1, **daf**-4, **daf**-7 and **daf**-8) do not. The increased life spans are suppressed completely by a **daf**-16 mutation and partially in a **daf**-2; **daf**-18 double mutant. A genetic pathway for determination of adult life span is presented based on the same strains and growth conditions used to characterize **Daf phenotypes**. Both dauer larva formation and adult life span are affected in **daf**-2; **daf**-12 double mutants in an allele-specific manner. Mutations in **daf**-12 do not extend adult life span, but certain combinations of **daf**-2 and **daf**-12 mutant alleles nearly quadruple it. This synergistic effect, which does not equivalently extend the fertile period, is the largest genetic extension of life span yet observed in a metazoan.

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L16 ANSWER 11 OF 82 MEDLINE
AN 95129796 MEDLINE
TI Multiple chemosensory defects in **daf**-11 and **daf**-21 mutants of **Caenorhabditis** elegans.
SO GENETICS, (1994 Oct) 138 (2) 303-16.
Journal code: 0374636. ISSN: 0016-6731.
AU Vowels J J; Thomas J H
AB **Phenotypic** analysis of the **daf**-11 and **daf**-21 mutants of **Caenorhabditis** elegans suggests that they have defects in components shared by processes analogous to vertebrate taste and olfaction. **daf**-11 and **daf**-21 mutations were previously shown to cause inappropriate response to the dauer-inducing pheromone. By mutational analysis and by disabling specific chemosensory sensilla with a laser, we show that neurons in the amphid sensilla are required for this pheromone response. Using behavioral assays, we find that **daf**-11 and **daf**-21 mutants are not defective in avoidance of certain non-volatile repellents, but are defective in taxis to non-volatile attractants. In addition, both mutants are defective in taxis to volatile attractants detected primarily by the amphid neuron AWC, but respond normally to volatile attractants detected primarily by AWA. We propose that **daf**-11 and **daf**-21 mediate sensory transduction for both volatile and non-volatile compounds in specific amphid neurons.

L16 ANSWER 15 OF 82 MEDLINE
AN 2000025937 MEDLINE
TI Control of **DAF**-7 TGF-(alpha) expression and neuronal process development by a receptor tyrosine kinase KIN-8 in **Caenorhabditis** elegans.
SO DEVELOPMENT, (1999 Dec) 126 (23) 5387-98.
Journal code: 8701744. ISSN: 0950-1991.
AU Koga M; Take-uchi M; Tameishi T; Ohshima Y
AB KIN-8 in **C. elegans** is highly homologous to human ROR-1 and 2 receptor tyrosine kinases of unknown functions. These kinases belong to a new subfamily related to the Trk subfamily. A kin-8 promoter::gfp fusion gene was expressed in ASI and many other neurons as well as in pharyngeal and head muscles. A kin-8 deletion mutant was isolated and showed constitutive dauer larva formation (**Daf**-c) **phenotype**: about half of the F(1) progeny became dauer larvae when they were cultivated on an old lawn of E. coli as food. Among the cells expressing kin-8::gfp, only ASI sensory neurons are known to express **DAF**-7 TGF-(beta), a key molecule preventing dauer larva formation. In the kin-8 deletion mutant, expression of **daf**-7::gfp in ASI was greatly reduced, dye-filling in ASI was specifically lost and ASI sensory processes did not completely extend into the amphid pore. The **Daf**-c **phenotype** was suppressed by **daf**-7 cDNA expression or a **daf**-3 null mutation. ASI-directed expression of kin-8 cDNA under the **daf**-7 promoter or expression by a heat shock promoter rescued the dye-filling defect, but not the **Daf**-c **phenotype**, of the kin-8 mutant. These results show that the kin-8 mutation causes the **Daf**-c **phenotype** through reduction of the **daf**-7 gene expression and that KIN-8 function is cell-autonomous for the dye-filling in ASI. KIN-8 is required for the process development of ASI, and also involved in promotion of **daf**-7 expression through a physiological or developmental function.

L16 ANSWER 21 OF 82 MEDLINE
AN 1999307426 MEDLINE
TI The PTEN tumor suppressor homolog in **Caenorhabditis** elegans regulates longevity and dauer formation in an insulin receptor-like signaling pathway.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Jun 22) 96 (13) 7427-32.
Journal code: 7505876. ISSN: 0027-8424.
AU Mihaylova V T; Borland C Z; Manjarrez L; Stern M J; Sun H
AB Inactivation of the tumor suppressor PTEN gene is found in a variety of human cancers and in cancer predisposition syndromes. Recently, PTEN protein has been shown to possess phosphatase activity on

phosphatidylinositol 3,4,5-trisphosphate, a product of phosphatidylinositol 3-kinase. We have identified a homolog of PTEN in **Caenorhabditis** elegans and have found that it corresponds to the **daf**-18 gene, which had been defined by a single, **phenotypically** weak allele, **daf**-18(e1375). By analyzing an allele, **daf**-18(nr2037), which bears a deletion of the catalytic portion of CePTEN/**DAF**-18, we have shown that mutation in **daf**-18 can completely suppress the dauer-constitutive **phenotype** caused by inactivation of **daf**-2 or age-1, which encode an insulin receptor-like molecule and the catalytic subunit of phosphatidylinositol 3-kinase, respectively. In addition, **daf**-18(nr2037) dramatically shortens lifespan, both in a wild-type background and in a **daf**-2 mutant background that normally prolongs lifespan. The lifespan in a **daf**-18(nr2037) mutant can be restored to essentially that of wild type when combined with a **daf**-2 mutation. Our studies provide genetic evidence that, in **C**. **elegans**, the PTEN homolog **DAF**-18 functions as a negative regulator of the **DAF**-2 and AGE-1 signaling pathway, consistent with the notion that **DAF**-18 acts a phosphatidylinositol 3,4,5-trisphosphate phosphatase in vivo. Furthermore, our studies have uncovered a longevity-promoting activity of the PTEN homolog in **C**. **elegans**.

L16 ANSWER 23 OF 82 MEDLINE
AN 1999102962 MEDLINE
TI The **C**. **elegans** PTEN homolog, **DAF**-18, acts in the insulin receptor-like metabolic signaling pathway.
SO MOLECULAR CELL, (1998 Dec) 2 (6) 887-93.
Journal code: 9802571. ISSN: 1097-2765.
AU Ogg S; Ruvkun G
AB An insulin-like signaling pathway, from the **DAF**-2 receptor, the AGE-1 phosphoinositide 3-kinase, and the AKT-1/AKT-2 serine/threonine kinases to the **DAF**-16 Fork head transcription factor, regulates the metabolism, development, and life span of **Caenorhabditis** elegans. Inhibition of **daf**-18 gene activity bypasses the normal requirement for AGE-1 and partially bypasses the need for **DAF**-2 signaling. The suppression of age-1 mutations by a **daf**-18 mutation depends on AKT-1/AKT-2 signaling, showing that **DAF**-18 acts between AGE-1 and the AKT input to **DAF**-16 transcriptional regulation. **daf**-18 encodes a homolog of the human tumor suppressor PTEN (MMAC1/TEP1), which has 3-phosphatase activity toward phosphatidylinositol 3,4,5-trisphosphate (PIP3). **DAF**-18 PTEN may normally limit AKT-1 and AKT-2 activation by decreasing PIP3 levels. The action of **daf**-18 in this metabolic control pathway suggests that mammalian PTEN may modulate insulin signaling and may be variant in diabetic pedigrees.

L16 ANSWER 24 OF 82 MEDLINE
AN 92120509 MEDLINE
TI Genetic analysis of chemosensory control of dauer formation in **Caenorhabditis** elegans.
SO GENETICS, (1992 Jan) 130 (1) 105-23.
Journal code: 0374636. ISSN: 0016-6731.
AU Vowels J J; Thomas J H
AB Dauer larva formation in **Caenorhabditis** elegans is controlled by chemosensory cells that respond to environmental cues. Genetic interactions among mutations in 23 genes that affect dauer larva formation were investigated. Mutations in seven genes that cause constitutive dauer formation, and mutations in 16 genes that either block dauer formation or result in the formation of abnormal dauers, were analyzed. Double mutants between dauer-constitutive and dauer-defective mutations were constructed and characterized for their capacity to form dauer larvae. Many of the genes could be interpreted to lie in a simple linear epistasis pathway. Three genes, **daf**-16, **daf**-18 and **daf**-20, may affect downstream steps in a branched part of the pathway. Three other genes, **daf**-2, **daf**-3 and **daf**-5, displayed partial or complex epistasis interactions that were difficult to interpret as part of a simple linear pathway. Dauer-defective mutations in nine genes cause structurally defective chemosensory cilia, thereby blocking chemosensation. Mutations in all nine of these genes appear to fall at a

single step in the epistasis pathway. Dauer-constitutive mutations in one gene, **daf**-11, were strongly suppressed for dauer formation by mutations in the nine cilium-structure genes. Mutations in the other six dauer-constitutive genes caused dauer formation despite the absence of functional chemosensory endings. These results suggest that **daf**-11 is directly involved in chemosensory transduction essential for dauer formation, while the other **Daf**-c genes play roles downstream of the chemosensory step.

L16 ANSWER 26 OF 82 MEDLINE
AN 96400917 MEDLINE
TI Genetic analysis of the roles of **daf**-28 and age-1 in regulating **Caenorhabditis** elegans dauer formation.
SO GENETICS, (1996 Jul) 143 (3) 1193-205.
Journal code: 0374636. ISSN: 0016-6731.
AU Malone E A; Inoue T; Thomas J H
AB Based on environmental cues, the nervous system of **Caenorhabditis** elegans regulates formation of the dauer larva, an alternative larval form specialized for long-term survival under harsh conditions. Mutations that cause constitutive or defective dauer formation (**Daf**-c or **Daf**-d) have been identified and the genes ordered in a branched pathway. Most **Daf**-c mutations also affect recovery from the dauer stage. The semi-dominant mutation **daf**-28(sa191) is **Daf**-c but has no apparent effect on dauer recovery. We use this unique aspect of **daf**-28(sa191) to characterize the effects of several **Daf**-d and synthetic **Daf**-c mutations on dauer recovery. We present double mutant analysis that indicates that **daf**-28(sa191) acts at a novel point downstream in the genetic pathway for dauer formation. We also show that **daf**-28(sa191) causes a modest increase (12-13%) in life span. The **phenotypes** and genetic interactions of **daf**-28(sa191) are most similar to those of **daf**-2 and **daf**-23 mutations, which also cause a dramatic increase in life span. We present mapping and complementation data that suggest that **daf**-23 is the same gene as age-1, identified previously by mutations that extend life span. We find that age-1 alleles are also **Daf**-c at 27 degrees.

L16 ANSWER 43 OF 82 MEDLINE
AN 84144794 MEDLINE
TI A pheromone-induced developmental switch in **Caenorhabditis** elegans: Temperature-sensitive mutants reveal a wild-type temperature-dependent process.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1984 Feb) 81 (3) 819-23.
Journal code: 7505876. ISSN: 0027-8424.
AU Golden J W; Riddle D L
AB Formation of a developmentally arrested dispersal stage called the dauer larva is enhanced by a **Caenorhabditis**-specific pheromone and is inhibited by increasing amounts of food. Pheromone-induced dauer larva formation of three tested wild-type strains is temperature-dependent, so that an increased percentage of the population forms dauer larvae at 25 degrees C compared to lower temperatures. Dauer-defective mutants fail to respond to added pheromone, and some behavioral mutants affected in thermotaxis or egg-laying also exhibit abnormal responses. Temperature-sensitive (ts) dauer-constitutive mutants form dauer larvae at a restrictive temperature regardless of environmental stimuli. At the permissive temperature (17.5 degrees C), alleles of six out of seven dauer-constitutive genes tested overrespond to the dauer-inducing pheromone. All known mutations in **daf**-4 (eight alleles) and **daf**-7 (five alleles) produce a ts dauer-constitutive **phenotype**. One **daf**-4 and one **daf**-7 allele are suppressed by the amber nonsense suppressor, sup-7(st5). At least these two dauer-constitutive mutations are likely to cause production of nonfunctional rather than ts gene products. These mutations appear to indirectly result in a ts **phenotype** by enhancing the expression of a wild-type ts developmental process.

L16 ANSWER 46 OF 82 MEDLINE
AN 94040749 MEDLINE
TI In search of new mutants in cell-signaling systems of the nematode

Caenorhabditis elegans. Review.
SO GENETICA, (1993) 88 (2-3) 137-46. Ref: 39
Journal code: 0370740. ISSN: 0016-6707.
AU Katsura I
AB Development of multicellular organisms is controlled mainly by cell-signaling systems. In this review I first discuss methods of genetic analysis and properties of mutants of cell-signaling systems in general and in the nematode **C. elegans**. Then, I describe two of our approaches to isolating new mutants in cell-signaling of **C. elegans**. The first approach is to select for mutants that have the same visible **phenotype** as those in known cell-signaling genes. In a survey of larval lethal mutations we found that there are quite a few mutants in which the inner surface of the body wall is detached from the outer surface of the intestine. Some of them map in genes that are known to act in cell-signaling systems in vulval induction or sex myoblast migration, which are not essential to the growth and survival of **C. elegans**. Therefore, we think many of the mutations of the above **phenotype** disrupt cell-signaling in an unidentified essential function, and also cell-signaling in the non-essential functions. The second approach is to isolate mutants resistant to a drug expected to disturb cell-signaling. As the drug we have chosen sodium fluoride, which depletes calcium ion, activates G-proteins and inactivates some phosphatases. The mutants are grouped into two classes (three and two genes, respectively) according to degree of fluoride-resistance and growth rate of larvae. Although there is so far no direct evidence that these mutants are related to cell-signaling, they show complex epistasis that can be explained by a model consisting of a cell-signaling pathway.

L16 ANSWER 50 OF 82 MEDLINE
AN 97048187 MEDLINE
TI Chemosensory neurons function in parallel to mediate a pheromone response in **C. elegans**.
SO NEURON, (1996 Oct) 17 (4) 719-28.
Journal code: 8809320. ISSN: 0896-6273.
AU Schackwitz W S; Inoue T; Thomas J H
AB Formation of the **C. elegans** dauer larva is repressed by the chemosensory neurons ADF, ASI, and ASG. Mutant analysis has defined two parallel genetic pathways that control dauer formation. By killing neurons in these mutants, we show that mutations in one of these genetic pathways disrupt dauer repression by ADF, ASI, and ASG. One gene in this pathway is **daf**-7, which encodes a TGFbeta-related protein. We find that **daf**-7::GFP fusions are expressed specifically in ASI and that expression is regulated by dauer-inducing sensory stimuli. We also show that a different chemosensory neuron, ASJ, functions in parallel to these neurons to induce dauer formation. Mutations in the second genetic pathway activate dauer formation in an ASJ-dependent manner. Thus, the genetic redundancy in this process is reflected at the neuronal level.

L16 ANSWER 54 OF 82 MEDLINE
AN 97067238 MEDLINE
TI Control of **C. elegans** larval development by neuronal expression of a TGF-beta homolog.
SO SCIENCE, (1996 Nov 22) 274 (5291) 1389-91.
Journal code: 0404511. ISSN: 0036-8075.
AU Ren P; Lim C S; Johnsen R; Albert P S; Pilgrim D; Riddle D L
AB The **Caenorhabditis** elegans dauer larva is specialized for dispersal without growth and is formed under conditions of overcrowding and limited food. The **daf**-7 gene, required for transducing environmental cues that support continuous development with plentiful food, encodes a transforming growth factor-beta (TGF-beta) superfamily member. A **daf**-7 reporter construct is expressed in the ASI chemosensory neurons. Dauer-inducing pheromone inhibits **daf**-7 expression and promotes dauer formation, whereas food reactivates **daf**-7 expression and promotes recovery from the dauer state. When the food/pheromone ratio is high, the level of **daf**-7 mRNA peaks during the L1 larval stage, when commitment to non-dauer development is made.

L16 ANSWER 58 OF 82 MEDLINE

AN 88167394 MEDLINE
TI Mutants of **Caenorhabditis** elegans that form dauer-like larvae.
SO DEVELOPMENTAL BIOLOGY, (1988 Apr) 126 (2) 270-93.
Journal code: 0372762. ISSN: 0012-1606.
AU Albert P S; Riddle D L
AB The development, ultrastructure, and genetics of two mutants that form dauer-like larvae have been characterized. Dauer larva morphogenesis is initiated regardless of environmental stimuli, and it is incomplete or abnormal. The resistance to detergent characteristic of normal dauer larvae is not fully achieved, and the mutants are unable to exit from the dauer-like state of developmental arrest. Mutant life span is not extended beyond the three weeks characteristic of the nondauer life cycle, whereas normal dauer larvae can live for several months. Growth of **daf**-15(m81)IV, the less dauer-like of the two, is nearly arrested at the second (dauer-specific) molt, but feeding is not completely suppressed. Head shape, cuticle, and intestinal ultrastructure are nondauer, whereas sensory structures (amphid and deirid) and excretory gland morphology are intermediate between that of dauer and nondauer stages. The **daf**-9(e1406)X mutant is dauer-like in head shape, cuticle, and deirid ultrastructure, intermediate in amphid and inner labial neuron morphology, and nondauer or abnormal in the intestine. Also, the **daf**-9 mutant exhibits abnormalities in the pharyngeal arcade cell processes and pharyngeal g1 gland. Double mutants carrying both **daf**-9 and **daf**-15 are more resistant to detergent than either single mutant. Like the single mutants, they cannot complete morphogenesis, and they are unable to exit from the dauer-like stage. Both **daf**-9 and **daf**-15 mutations are epistatic to previously described dauer-defective mutations, indicating that these two genes act late in the pathway leading to the dauer larva. The genetic tests and the mutant ultrastructure suggest that the two genes may affect parallel pathways of morphogenesis.

L16 ANSWER 69 OF 82 MEDLINE
AN 95365402 MEDLINE
TI Thermotolerance and extended life-span conferred by single-gene mutations and induced by thermal stress.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Aug 1) 92 (16) 7540-4.
Journal code: 7505876. ISSN: 0027-8424.
AU Lithgow G J; White T M; Melov S; Johnson T E
AB We have discovered that three longevity mutants of the nematode **Caenorhabditis** elegans also exhibit increased intrinsic thermotolerance (Itt) as young adults. Mutation of the age-1 gene causes not only 65% longer life expectancy but also Itt. The Itt **phenotype** cosegregates with age-1. Long-lived spe-26 and **daf**-2 mutants also exhibit Itt. We investigated the relationship between increased thermotolerance and increased life-span by developing conditions for environmental induction of thermotolerance. Such pretreatments at sublethal temperatures induce significant increases in thermotolerance and small but statistically highly significant increases in life expectancy, consistent with a causal connection between these two **traits**. Thus, when an animal's resistance to stress is increased, by either genetic or environmental manipulation, we also observe an increase in life expectancy. These results suggest that ability to respond to stress limits the life expectancy of **C. elegans** and might do so in other metazoa as well.

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(FILE 'HOME' ENTERED AT 18:07:47 ON 09 JAN 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 18:07:56 ON 09 JAN 2003

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L1         12645 S C. ELEGANS
L2         28518 S C. ELEGANS OR CAENORHABDITIS
L3          4937 S L2 AND (TRAIT OR PHENOTYP? OR SCREEN?)
L4           557 S L3 AND LIBRAR?
L5           288 DUP REM L4 (269 DUPLICATES REMOVED)
L6           288 FOCUS L5 1-
L7         34508 S ELEGANS OR NEMATODE (L) PHENOTYPIC PROFILES
L8             1 S (ELEGANS OR NEMATODE) (L) PHENOTYPIC PROFILES
L9          5548 S (ELEGANS OR NEMATODE) (L) MUTANT?
L10          587 S L9 AND SCREEN?
L11          269 S L10 AND PHENOTYP?
L12          119 DUP REM L11 (150 DUPLICATES REMOVED)
L13          119 FOCUS L12 1-
L14          192 S L3 AND DAF?
L15           82 DUP REM L14 (110 DUPLICATES REMOVED)
L16           82 FOCUS L15 1-
                 E BOGAERT THIERRY?/AU
                 E BOGAERT T?/AU
L17           29 S E4
L18           28 DUP REM L17 (1 DUPLICATE REMOVED)
L19           28 SORT L18 PY
L20           23 S L19 AND L2

=> d an ti so au ab pi l20 13 15 16 18

L20  ANSWER 13 OF 23  CAPLUS  COPYRIGHT 2003 ACS
AN   2000:756909  CAPLUS
DN   133:317531
TI   Nematodes for screening of compounds with potential pharmacological
     activity
SO   PCT Int. Appl., 137 pp.
     CODEN: PIXXD2
IN   Verwaerde, Philippe; Platteeuw, Christ; Cuvillier, Gwladys; Bogaert,
     Thierry
AB   Screening methods are provided which use nematode worms, particularly but
     not exclusively Caenorhabditis elegans , which are adapted to be
     performed in a high-throughput format.
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2000063427     A2   20001026      WO 2000-IB575    20000414
     WO 2000063427     A3   20011206
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
             IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
             SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
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     GB 2359358        A1   20010822      GB 2001-11712    20000414
     GB 2359358        B2   20020327
     GB 2359359        A1   20010822      GB 2001-11713    20000414
     GB 2359359        B2   20020123
     GB 2359360        A1   20010822      GB 2001-11783    20000414
     GB 2359360        B2   20020116
     GB 2359361        A1   20010822      GB 2001-11787    20000414
     GB 2359361        B2   20020116
     GB 2359626        A1   20010829      GB 2001-11714    20000414
     GB 2359626        B2   20020501
     GB 2359627        A1   20010829      GB 2001-11778    20000414
     GB 2359627        B2   20020123
     EP 1175506        A2   20020130      EP 2000-920972   20000414
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
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JP 2002542466 T2 20021210 JP 2000-612504 20000414

L20 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2000:756907 CAPLUS
DN 133:317530
TI Drug screening using modified nematode worms
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN Verwaerde, Philippe; Feichtinger, Richard; Beghyn, Myriam; **Bogaert, Thierry**
AB The invention provides methods of screening compds. for potential pharmacol. activity using nematode worms, principally but not exclusively, the nematode **Caenorhabditis** elegans. Specifically, the invention relates to the use of nematodes modified to have certain characteristics which provide advantages for compd. screening, such as constitutive pharyngeal pumping, increased gut permeability or altered gut mol. transport. Methods for selecting suitably modified nematodes from a population of nematodes are also provided.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000063425	A2	20001026	WO 2000-IB557	20000414
WO 2000063425	A3	20010308		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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GB 2351152	A1	20001220	GB 2000-9360	20000414
GB 2351152	B2	20010725		
GB 2358399	A1	20010725	GB 2001-9262	20000414
GB 2358399	B2	20020116		
GB 2358400	A1	20010725	GB 2001-9263	20000414
GB 2358400	B2	20020116		
EP 1169472	A2	20020109	EP 2000-919101	20000414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002542465	T2	20021210	JP 2000-612502	20000414

L20 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2000:756906 CAPLUS
DN 133:317529
TI Method for screening compounds using nematode worms
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
IN Feichtinger, Richard; Rottiers, Veerle; **Bogaert, Thierry**; Maillet, Isabelle
AB The invention provides improved methods of screening compds. for potential pharmacol. activity using nematode worms, principally but not exclusively, **Caenorhabditis** elegans. Specifically, the invention relates to methods in which the test compd. is added directly to a nematode food source organism (e.g. a microorganism) and therefore taken up by the nematodes during feeding.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000063424	A2	20001026	WO 2000-IB554	20000414
WO 2000063424	A3	20010208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2350896	A1	20001213	GB 2000-9364	20000414

GB 2350896 B2 20010425
EP 1169471 A2 20020109 EP 2000-919099 20000414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002542464 T2 20021210 JP 2000-612501 20000414

L20 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2000:401965 CAPLUS
DN 133:28275
TI Method for constructing libraries of phenotypic profiles in nematode worm
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
IN Kaletta, Titus; Feichtinger, Richard; Van Poucke, Jonas; Van Geel, Anton; Appelmans, Saskia; Van Criekinge, Wim; **Bogaert, Thierry**
AB Methods are provided for use in constructing libraries of phenotypic profiles in a nematode worm such as **Caenorhabditis** elegans. The methods require measurement of identifiable characteristics of the worm and systematic scoring of these characteristics. Also provided are methods of identifying compds. with potential pharmacol. activity, for detg. the mode of action of a given compd. and for assigning genes to particular biochem. pathways.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000034438	A2	20000615	WO 1999-EP9710	19991207
WO 2000034438	A3	20001109		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1137754	A2	20011004	EP 1999-963460	19991207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531115	T2	20020924	JP 2000-586872	19991207

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L Number	Hits	Search Text	DB	Time stamp
37	1816	c ADJ elegans	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:24
43	29	c ADJ elegans.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:23
55	321	c ADJ elegans and (phenoty$5 SAME screen$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:37
61	17	bogaert NEAR thierry	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:37
67	2	Feichtinger NEAR richard	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:35
75	1	kaletta NEAR titus	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:40
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117	0	(constructing ADJ libraries) SAME elegans	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:45
123	310	librar$5 SAME elegans	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:49
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141	4	leastone and gene	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/09 17:51
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175	13	((US-6225120-$ or US-6278039-$ or US-6329566-$ or US-6433247-$ or US-6465715-$).did. or (US-20010016332-$ or US-20020037585-$ or US-20020064523-$ or US-20020194624-$).did. or (WO-9638555-$ or WO-9824810-$ or WO-9937770-$ or GB-2349217-$ or WO-9964586-$ or GB-2351496-$ or GB-2358399-$ or GB-2358400-$ or GB-2359358-$ or WO-9851351-$ or WO-9630053-$).did. or (GB-2359361-$ or GB-2359358-$ or GB-2351152-$).did.) and phenoty$5	USPAT; US-PGPUB; EPO; DERWENT	2003/01/09 18:03